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EXAMINER	
YANG, NELSON C	
ART UNIT	PAPER NUMBER
1641	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/963,232	BURCH ET AL.	
	Examiner	Art Unit	
	Nelson Yang	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 June 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24,28-32 and 34-94* is/are pending in the application.

4a) Of the above claim(s) *1-23, 41,42,44-91* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *24,28-32,34-40,43 and 92-94* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of claims 24-43, 92-94 in Paper No. 4 is acknowledged.

2. Applicant's cancellation of claims 25-27, and 33 in Paper No. 4 are acknowledged.

3. Claims 41 and 42 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 4.

Specification

4. The disclosure is objected to because of the following informalities:

5. On page 1, line 24, the word "to" may be needed between "which apply" and "the three dimensional".

6. On page 18, lines 23-24, the sentence "*In vitro immunization* is preferred if the analog-carrier conjugates would be subject to metabolic decomposition, *in vivo*" is ambiguous. It is not clear whether applicant is referring to in vitro or in vivo immunization if analog-carrier conjugates would be subject to metabolic decomposition.

Appropriate correction is required.

7. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The range of the dissociation constant is not found in the specification. If the subject matter claimed is already in the specification, it would be appreciated if applicant

could direct examiner to the portion of the specification where they are discussed. Otherwise, applicant should correct the lack of written description in the specification.

8. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The subject matter claimed in claims 36 and 37 cannot be found in the specification. If the subject matter claimed is already in the specification, it would be appreciated if applicant could direct examiner to the portion of the specification where they are discussed. Otherwise, applicant should correct the lack of written description in the specification.

Claim Objections

9. The numbering of claims is not in accordance with 37 CFR 1.126 which requires the original numbering of the claims to be preserved throughout the prosecution. When claims are canceled, the remaining claims must not be renumbered. When new claims are presented, they must be numbered consecutively beginning with the number next following the highest numbered claims previously presented (whether entered or not).

Misnumbered claims 44-46 have been renumbered as 92-94, respectively.

10. A series of singular dependent claims is permissible in which a dependent claim refers to a preceding claim which, in turn, refers to another preceding claim.

A claim which depends from a dependent claim should not be separated by any claim which does not also depend from said dependent claim. It should be kept in mind that a dependent claim may refer to any preceding independent claim. In general, applicant's sequence will not be changed. See MPEP § 608.01(n).

Claim Rejections - 35 USC § 112

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 29, 39, and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear what the exact range is being specified by the phrase "about 0.01 nM to about 10 nM". This could refer to values less than .01 nM and values greater 10 nM, such as .000001 nM and 15 nM, depending on how the word "about" was interpreted. This also applies to claims 39 and 40, in regard to the word "approximately".

12. Claim 36 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear whether the word "pooled" is meant to mean that the antibodies are mixed together or if they somehow remain in distinct groups or if something else is meant by the term "pooled". The claim is currently interpreted to mean that the antibodies are mixed together.

13. Claim 37 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is not clear how each member of the panel of monoclonal antibodies can be utilized separately, particularly if the antibodies have been mixed together and attached to a support. The claim is currently interpreted to mean that each type of the monoclonal antibodies is to be analyzed separately.

Claim Rejections - 35 USC § 102

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

15. Claims 24, 28, 31, 32, 34, 36-40, 43, and 92-94 are rejected under 35 U.S.C. 102(e) as being anticipated by Kauvar et al [US 5,674,688]. Specifically, Kauvar et al teaches identifying one or more key component fragments of one or more chemical compounds having binding affinity for a target receptor wherein said key component fragment is a portion of a molecule which contributes to the binding affinity of that molecule for the target receptor (claim 1), coupling one or more analogs of the compounds to a carrier molecule to construct one or more analog-carrier conjugates (column 8, lines 25-55), utilizing the analog-carrier conjugates to generate a panel of monoclonal antibodies *in vitro* and *in vivo* (column 8-9, lines 1-21 and example 1), assaying the monoclonal antibodies to determine specificity (claim 11), immobilizing the monoclonal antibodies on a support (column 7-8, lines 41-45 and preparation A), conducting a series of in-vitro assays utilizing said immobilized antibodies to screen one or more compounds of interest (columns 9-11, examples 1-2). Kauvar et al further teaches identifying one or more key component fragments of one or more chemical compounds having binding affinity for a target receptor wherein said key component fragment is a portion of a molecule which contributes to the binding affinity of that molecule for the target receptor (claim

1), coupling one or more analogs of the compounds to a carrier molecule to construct one or more analog-carrier conjugates (column 8, lines 25-55), utilizing two or more analog-carrier conjugates to generate a panel of monoclonal antibodies (column 8-9, example 1, claims 1, 2, 11-12), assaying the monoclonal antibodies to determine specificity and binding affinities (column 2, lines 21-51, claim 11), immobilizing the monoclonal antibodies on a support (column 7-8, lines 41-45 and preparation A), conducting a series of in-vitro assays utilizing said immobilized antibodies to screen one or more compounds of interest (columns 9-11, examples 1-2).

16. With respect to claim 28, monoclonal antibodies for each analog-carrier conjugate exhibiting the strongest binding are included in a panel (column 5, line 46 – column 7, line 28).

17. With respect to claims 31, the monoclonal antibodies can be generated *in vitro* (column 7, line 63-67 and column 8-9, lines 1-21 and example 1).

18. With respect to claim 32, the analog-carrier conjugates are constructed using an amino functional group (column 8, example 1).

19. With respect to claim 34, the carrier molecule is Keyhole Limpet Hemocyanin (KLH) (column 7, line 63 – column 8, line 21).

20. With respect to claim 36, the panel of monoclonal antibodies is pooled before attachment to support (column 5, lines 8-27).

21. With respect to claim 37, the antibodies are utilized separately (claim 1, 10, 11).

22. With respect to claim 38, atrazine, simazine prometon are organic compounds (column 8, table 1).

23. With respect to claim 39 and 40, the method of Kauvar is used to detect altrazine (215.69), which has a molecular weight less than 500 g/mole (column 8, table 1).

24. With respect to claim 43, the panel of Kauvar is composed of 2-20 monoclonal antibodies (column 8, example 1, column 9, lines 40-42, claim s1, 20).

25. With respect to claim 92, the compounds of interest are synthetic products (herbicides) [column 8, table 1]

26. Claims 24, 28, 30, 32, 35-40, 43, 92 are rejected under 35 U.S.C. 102(e) as being anticipated by Buechler et al [US 5,939,272]. Buechler teaches an assay for an analyte which may be detected by the formation of a complex between a ligand and another substance capable of specific interaction with that ligand, i.e. ligand receptor. The ligand may be the ligand itself or a substance which, if detected can be used to infer the presence of the analyte in the sample.

Specifically, Buechler teaches the steps of identifying one or more key component fragments (Fc fragment of mouse IgG), measuring the dissociation constant for the binding of the monoclonal antibodies to the analogs to determine which monoclonal antibodies exhibit the strongest binding (column 14-16, column 33, example 3 and 4), immobilizing the monoclonal antibodies having the strongest binding on a support (column 33, example 3, specifically lines 24-26). Buechler et al suggests that these in-vitro assays utilizing said immobilized monoclonal antibodies could be used to screen one or more compounds of interest (column 1, lines 53-56).

Buechler et al does not teach the step of coupling one or more analogs of the one or more chemical compounds to a carrier molecule. However, Buechler et al does teach the coupling of one or more analogs of the one or more chemical compounds to an enzyme (column 8, lines 60-65), which could be considered to be a macromolecule capable of being recognized by the immune system. Furthermore, Buechler discloses haptens as an example of a ligand (column 2,

lines 17-19). Since a person of ordinary skill in the art would know that haptens are small molecules that are unable to react with antibodies by themselves, and need to be conjugated to a carrier molecule in order to be able to do so [Encyclopedia Britannica, under *hapten*], it would be clear that Buechler intended to couple hapten analogs of the one or more chemical compounds to a carrier molecule to construct one or more analog-carrier conjugates.

27. With respect to claim 28, Buechler teaches the application of the assay toward an assay for a drugs of abuse panel consisting of antibodies representing each analog-carrier conjugate (column 38, example 110).

28. With respect to claims 30, Buechler does not specify whether the monoclonal antibodies must be generated *in vivo* or *in vitro*, but he does disclose an embodiment in which antibodies are generated *in vivo* (column 38, lines 35-40).

29. With respect to claim 32, Buechler discloses various embodiments of the invention involving analog-carrier conjugates with amino functional groups (columns 39-40, example 13, column 45, example 19).

30. With respect to claim 35, Buechler suggests a chemical compound that exhibits opiate activity (opiates) (column 30, line 2).

31. With respect to claim 36, in the assay for drugs of abuse panel Buechler discloses, the monoclonal antibodies are pooled before attachment to a support (column 38, lines 54-67, column 39, lines 1-4).

32. With respect to claim 37, each type of monoclonal antibodies in the panel is analyzed separately to screen compounds of interest (column 39, lines 26-29).

33. With respect to claim 38, Buechler suggests one or more chemical compounds that are organic molecules (ovulatory steroids) (column 29, lines 65-67).

34. With respect to claims 39 and 40, Buechler discloses an embodiment of the invention using estrone-3-glucuronide (11.2 mg, 25μM) as the chemical compound, which has a molecular weight of less than 500 g/mole (column 32, lines 49-57).

35. With respect to claim 43, Buechler suggests a drugs abuse panel comprised of monoclonal antibodies to at least five drugs (column 38, lines 22-30).

36. With respect to claim 92, Buechler suggests synthetic products such as therapeutic drugs and toxic drugs (column 1, line 55-58) as examples of compounds of interest for *in vitro* screening.

Claim Rejections - 35 USC § 103

37. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kauvar et al [US 5,674,688]. The method of Kauvar as disclosed above fails to recite the specific feature of generating monoclonal antibodies with a dissociation constant in the range of 0.01 nM to 10 nM. However, it would have been obvious for a person of ordinary skill in the art to generate monoclonal antibodies with dissociation constants within this particular range to achieve

monoclonal antibodies having the strongest binding, because it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. At 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since applicant has not disclosed that the specific limitations recited in instant claim 29 are for any particular purpose or to solve any stated problem and the prior art discloses that additional methods for conducting assays designed to detect and measure binding are used to create the SC profiles, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the dissociation constants of the monoclonal antibodies in the method disclosed by Kauvar et al by normal optimization procedures known in the art.

38. Claim 30 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kauvar et al [US 5,674,688] in view of Harlow [Antibodies: A Laboratory Manual]. The method disclosed by Kauvar does not specify whether the monoclonal antibodies must be generated *in vivo* or *in vitro*, but he does disclose an embodiment in which antibodies are generated *in vitro* (column 7, line 63-67 and column 8-9, lines 1-21 and example 1). However, methods of generating monoclonal antibodies *in vivo* would be well known to a person of ordinary skill in the art as well, as taught by Harlow.

39. Claim 35 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kauvar et al [US 5,939,272] in view of Buechler et al [US 5,939,272]. The method of Kauvar fails to disclose the use of chemical compounds that exhibit PDEIV inhibitor or opiate activity. Buechler suggests a chemical compound that exhibits opiate activity (opiates), for the purpose of creating a drugs of abuse panel (column 30, line 2, column 38, example 11). Therefore it would have been obvious for a person of ordinary skill in the art to use the method of Kauvar to test for chemical counds that exhibit opiate activity.

40. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Buechler et al [US 5,939,272]. The method of Buechler as disclosed above fails to recite the specific feature of a dissociation constant in the range of 0.01 nM to 10 nM. However, it would have been obvious for a person of ordinary skill in the art to adjust the dissociation constant within this particular range to achieve monoclonal antibodies having the strongest bonding, because it has long been settled to be no more than routine experimentation for one of ordinary skill in the art to discover an optimum value of a result effective variable. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum of workable ranges by routine experimentation." Application of Aller, 220 F.2d 454, 456, 105 USPQ 233, 235-236 (C.C.P.A. 1955). "No invention is involved in discovering optimum ranges of a process by routine experimentation." Id. At 458, 105 USPQ at 236-237. The "discovery of an optimum value of a result effective variable in a known process is ordinarily within the skill of the art." Application of Boesch, 617 F.2d 272, 276, 205 USPQ 215, 218-219 (C.C.P.A. 1980). Since applicant has not disclosed that the specific limitations recited in instant claim 29 are for any

particular purpose or to solve any stated problem and the prior art teaches that the dissociation of the ligand analogue conjugate: antibody complex becomes the rate limiting step (involving the dissociation constant), and that the maximum response is used to calculate the ratio of free to bound ligand analogue conjugate for the unknown response, absent unexpected results, it would have been obvious for one of ordinary skill to discover the optimum workable ranges of the dissociation constants of the monoclonal antibodies in the method disclosed by Buechler et al by normal optimization procedures known in the art.

41. Claim 31 is rejected under 35 U.S.C. 103(a) as being unpatentable over Buechler et al [US 5,939,272] in view of Keiser [*Monoclonal antibodies against human low density lipoprotein*, Keiser, Matrix Vol. 10 (1990), pg 97]. The method disclosed by Buechler does not specify whether the monoclonal antibodies must be generated *in vivo* or *in vitro*, but he does disclose an embodiment in which antibodies are generated *in vivo* (column 38, lines 35-40). However, methods of generating monoclonal antibodies *in vitro* would be well known to a person of ordinary skill in the art as well (section 2.2. monoclonal antibodies against LDL). Furthermore, it is not clear if there would be any distinct advantage to using monoclonal antibodies generated *in vivo* as opposed to monoclonal antibodies generated *in vitro*.

42. Claim 34 is rejected under 35 U.S.C. 103(a) as being unpatentable over Buechler et al [US 5,939,272] in view of Harlow et al [Keyhole Limpet Hemocyanin, *Calbiochem®*, adapted from *Immunochemistry Labfax*] and Kauvar et al [US 5,674,688]. Buechler does not specify the use of Keyhole Limpet Hemocyanin, ovalbumin or thryoglobulin. However, Keyhole Limpet Hemocyanin is a well-known carrier protein, and is commonly sold by companies as a carrier

protein used in the preparation of hapten conjugates. Therefore, it would be obvious to a person of ordinary skill in the art to use KLH as a carrier molecule.

Response to Remarks

43. Applicant's remarks with respect to the parent application have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

44. No claims are allowed.

45. The following references are also cited as art of interest: Kauvar et al [US 5,338,659], Ax et al [US 5,962,241], Kamada et al [US 6,140,474], Milne, RW; Marcel, YL; *Monoclonal antibodies against human low density lipoprotein*, 1982, FEBS Letters, 146(1), p.97-100, Keiser, HD; *Monoclonal Antibodies Reacting with Tryptic Hyaluronic Acid-Binding Region and Link Protein Fragments of Bovine Nasal Cartilage Proteoglycan*, 1990, Matrix, 10, p.131-137, Sunderland, CA; McMaster, WR; Williams, AF; *Purification with monoclonal antibody of a predominant leukocyte-common antigen and glycoprotein from rat thymocytes*; 1979, Eur. J. Immunol., 9, p.155-159.

46. The Group and/or Art Unit location of your application in the PTO has changed. To aid in the correlating of any papers for this application, all further correspondence should be directed to Group Art Unit 1641.

47. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nelson Yang whose telephone number is 703-305-4508. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V Le can be reached on 703-305-3399. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

NY

LONG V. LE
SUPERVISORY PATENT EXAMINER
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08/22/03